Appendix 1

14 ANSWER 5 OF 12 MEDLINE on STN DUPLICATE 3
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TITLE: Roles of two VEGF receptors, Flt-1 and KDR, in the signal transduction of VEGF effects in human vascular endothelial cells.
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AB Vascular endothelial growth factor (VEGF) is a principal regulator of vasculogenesis and angiogenesis. VEGF expresses its effects by binding to two VEGF receptors, Flt-1 and KDR. However, properties of Flt-1 and KDR in the signal transduction of VEGF-mediated effects in endothelial cells (ECs) were not entirely clarified. We investigated this issue by using two newly developed blocking monoclonal antibodies (mAbs) against Flt-1 and KDR. VEGF elicits DNA synthesis and cell migration of human umbilical vein endothelial cells (HUVECs). The pattern of inhibition of these effects by two mAbs indicates that DNA synthesis is preferentially mediated by KDR. In contrast, the regulation of cell migration by VEGF appears to be more complicated. Flt-1 regulates cell migration through modulating actin reorganization, which is essential for cell motility. A distinct signal is generated by KDR, which influences cell migration by regulating cell adhesion via the assembly of vinculin in focal adhesion plaque and tyrosine-phosphorylation of focal adhesion kinase (FAK) and paxillin.